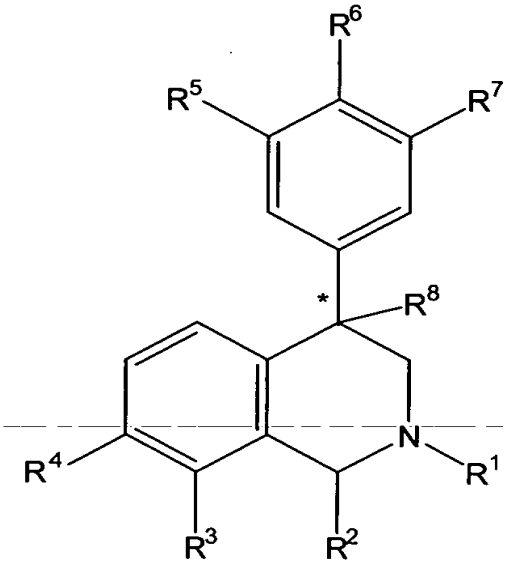

IA-IF

wherein:

the carbon atom designated * is in the R or S configuration;

R^1 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl or C_4-C_7 cycloalkylalkyl, each of which is optionally substituted with 1 to 3 substituents independently selected at each occurrence thereof from C_1-C_3 alkyl, halogen, aryl, -CN, OR^9 and $-NR^9R^{10}$;

R^2 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_4-C_7 cycloalkylalkyl or C_1-C_6 haloalkyl;

R^3 is H, halogen, $-OR^{11}$, $-S(O)_nR^{12}$, $-S(O)_nNR^{11}R^{12}$, -CN, $-C(O)R^{12}$, $-C(O)NR^{11}R^{12}$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_4-C_7 cycloalkylalkyl, -O(phenyl) or -O(benzyl), wherein each of -O(phenyl) and -O(benzyl) is optionally substituted from 1 to 3 times with a substituent selected independently at each occurrence thereof from halogen, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl, or C_1-C_4 alkoxy, or wherein R^3 is a C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl or C_4-C_7 cycloalkylalkyl group, then said group is optionally substituted with from 1 to 3 substituents selected independently at each occurrence thereof from C_1-C_3 alkyl, halogen, aryl, -CN, $-OR^9$ and $-NR^9R^{10}$; provided that for compounds of formula IA, R^3 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl or C_4-C_7 cycloalkylalkyl, each of which is optionally

substituted with from 1 to 3 substituents selected independently at each occurrence thereof from C_1-C_3 alkyl, halogen, aryl, -CN, -OR^9 and -NR^9R^{10};

provided that for compounds of formula IB, R^3 is -O(phenyl), -O(benzyl), -$OC(O)R^{13}$ or $S(O)_nR^{12}$, each of -O(phenyl) and -O(benzyl) is optionally substituted from 1 to 3 times with a substituent selected independently at each occurrence thereof from halogen, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl, or C_1-C_4 alkoxy;

R^4 is H, halogen, -OR^{11}, -$S(O)_nR^{12}$, -$S(O)NR^{11}R^{12}$, -CN, -$C(O)R^{12}$, -$C(O)NR^{11}R^{12}$, -$NR^{11}R^{12}$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_4-C_7 cycloalkylalkyl, -O(phenyl) or -O(benzyl), wherein each of -O(phenyl) and -O(benzyl) is optionally substituted from 1 to 3 times with a substituent selected independently at each occurrence thereof from halogen, cyano, C_1-C_4 alkyl, C_1-C_4 halolkyl, or C_1-C_4 alkoxy and wherein R^4 is a C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl or C_4-C_7 cycloalkylalkyl group, then said group is optionally substituted with from 1 to 3 substituents selected independently at each occurrence thereof from C_1-C_3 alkyl, halogen, aryl, -CN, -OR^9 and -NR^9R^{10}; provided that for compounds of formula IC, R^4 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl or C_4-C_7 cycloalkylalkyl, each of which is optionally substituted; provided that for compounds of formula ID, R^4 is -O(phenyl), -O(benzyl), -$OC(O)R^{13}$, -$NR^{11}R^{12}$ or -$S(O)_nR^{12}$, each of -O(phenyl) and -O(benzyl) being optionally substituted, wherein R^3 and R^4 are not both H;

R^5, R^6 and R^7 in compounds of each of the formulae IA, IB, IC, ID, IE and IF are each independently H, halogen, -OR^{11}, -$S(O)_nR^{12}$, -CN, -$C(O)R^{12}$, -$NR^{11}R^{12}$, -$C(O)NR^{11}R^{12}$, -$NR^{11}C(O)R^{12}$, -$NR^{11}C(O)_2R^{12}$, -$NR^{11}C(O)NR^{12}R^{13}$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl or C_4-C_7 cycloalkylalkyl, wherein each of R^5, R^6 and R^7 is a C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl or C_4-C_7 cycloalkylalkyl group, then said group is optionally substituted with from 1 to 3 substituents selected independently at each occurrence thereof from C_1-C_3 alkyl, halogen, aryl, -CN, -OR^9 and -NR^9R^{10}, or R^5 and R^6 or R^6 and R^7 may be -O-$C(R^{12})_2$-O-; provided that for compounds of formula IE at least one of R^5 or R^7 is fluoro, chloro, or methyl; or R^5 or R^6 are each independently -O-$C(R^{12})_2$-O- in compounds of the formulae IE, but only where R^7 is fluoro, chloro or methyl; or R^7 and R^6 can independently also be -O-$C(R^{12})_2$-O- in compounds of the formulae IE, but only where R^5 is fluoro, chloro or methyl;

R^8 is H or halogen, provided that for compounds of formula IF, R^8 is halogen;

R^9 and R^{10} are each independently H, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxyalkyl, C_3-C_6 cycloalkyl, C_4-C_7 cycloalkylalkyl, -C(O)R^{13}, phenyl or benzyl, where phenyl or benzyl is optionally substituted from 1 to 3 times with a substituent selected independently at each occurrence thereof from halogen, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl, or C_1-C_4 alkoxy; or R^9 and R^{10} are taken together with the nitrogen to which they are attached to form piperideine, pyrrolidine, piperazine, N-methylpiperazine, morpholine, or thiomorpholine;

R^{11} is H, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxyalkyl, C_3-C_6 cycloalkyl, C_4-C_7 cycloalkylalkyl, -C(O)R^{13}, phenyl or benzyl, where R^{11} is a C_1-C_4 alkyl, phenyl or benzyl group, then said group is optionally substituted from 1 to 3 times with a substituent selected independently at each occurrence thereof from halogen, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl, or C_1-C_4 alkoxy;

R^{12} is H, amino, C_1-C_4 alkyl, (C_1-C_4 alkyl)amino, C_1-C_4 haloalkyl, C_1-C_4 alkoxyalkyl, C_3-C_6 cycloalkyl, C_4-C_7 cycloalkylalkyl, phenyl or benzyl, where phenyl or benzyl is optionally substituted from 1 to 3 times with a substituent selected independently from halogen, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl and C_1-C_4 alkoxy; or R^{11} and R^{12} are taken together with the nitrogen to which they are attached to form piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine, or thiomorpholine;

provided that only one of R^9 and R^{10} or R^9 and R^{10} are taken together with the nitrogen to which they are attached to form piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine, or thiomorpholine;

R^{13} is C_1-C_4 alkyl, C_1-C_4 haloalkyl or phenyl;

n is 0, 1, or 2, and;

aryl is phenyl which is optionally substituted 1-3 times with halogen, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl and C_1-C_4 alkoxy, or

an oxide thereof, or a pharmaceutically acceptable salt thereof, wherein the compound has a binding affinity for dopamine transporter protein to a binding affinity for norepinephrine transporter protein ratio of at least 2:1 and a binding affinity for serotonin transporter protein to a binding affinity for norepinephrine transporter protein ratio of at least 20:1.

a^3 14. (Amended) The compound of claim 1, wherein R^3 and R^4 are each halogen.

a^4 30. (Amended) A compound according to claim 1, selected from the group consisting of the following compounds:

2,7-dimethyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;
4-(4-methoxy)phenyl-2,7-dimethyl-1,2,3,4-tetrahydroisoquinoline;
2,7-dimethyl-4-(4-fluoro)phenyl-1,2,3,4-tetrahydroisoquinoline;
2,7-dimethyl-4-(3-fluoro)phenyl-1,2,3,4-tetrahydroisoquinoline;
4-(3,4-difluoro)phenyl-2,7-dimethyl-1,2,3,4-tetrahydroisoquinoline;
2,7-dimethyl-4-(4-fluoro-3-methyl)phenyl-1,2,3,4-tetrahydroisoquinoline;
4-(3-chloro-4-fluoro)phenyl-2,7-dimethyl-1,2,3,4-tetrahydroisoquinoline;
4-(3-chloro)phenyl-2,7-dimethyl-1,2,3,4-tetrahydroisoquinoline;
2,7-dimethyl-4-(4-methyl)phenyl-1,2,3,4-tetrahydroisoquinoline;
2,7-dimethyl-4-(3-fluoro-4-methyl)phenyl-1,2,3,4-tetrahydroisoquinoline;
4-(4-chloro)phenyl-2,7-dimethyl-1,2,3,4-tetrahydroisoquinoline;
4-(4-chloro-3-fluoro)phenyl-2,7-dimethyl-1,2,3,4-tetrahydroisoquinoline;
4-(3,4-dichloro)phenyl-2,7-dimethyl-1,2,3,4-tetrahydroisoquinoline;
7-ethyl-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;
4-(3,4-difluoro)phenyl-7-ethyl-2-methyl-1,2,3,4-tetrahydroisoquinoline;
7-fluoro-4-(4-methoxy)phenyl-2-methyl-1,2,3,4-tetrahydroisoquinoline;
7-fluoro-4-(3-fluoro-4-methoxy)phenyl-2-methyl-1,2,3,4-tetrahydroisoquinoline;
7-fluoro-4-(3-fluoro-4-methyl)phenyl-2-methyl-1,2,3,4-tetrahydroisoquinoline;
7-fluoro-4-(4-chloro-3-fluoro)phenyl-2-methyl-1,2,3,4-tetrahydroisoquinoline;
4-(3,4-difluoro)phenyl-7-fluoro-2-methyl-1,2,3,4-tetrahydroisoquinoline;
4-(3-chloro)phenyl-7-fluoro-2-methyl-1,2,3,4-tetrahydroisoquinoline;
7-cyano-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;
2-methyl-4-phenyl-7-trifluoromethyl-1,2,3,4-tetrahydroisoquinoline;
4-phenyl-1,2,7-trimethyl-1,2,3,4-tetrahydroisoquinoline;
4-phenyl-2,7,8-trifluoromethyl-1,2,3,4-tetrahydroisoquinoline;
2,7-dimethyl-8-fluoro-4-phenyl-1,2,3,4-tetrahydroisoquinoline;
2,8-dimethyl-7-fluoro-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

a4

2,7-dimethyl-8-methoxy-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

2,7-dimethyl-8-hydroxy-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

2-methyl-4-phenyl-7-trifluoromethoxy-1,2,3,4-tetrahydroisoquinoline;

4-(3,4-difluoro)phenyl-7-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline;

4-(4-fluoro-3-methyl)phenyl-7-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline;

4-(3-fluoro-4-methyl)phenyl-7-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline;

7-methoxy-4-(3-methyl)phenyl-2-methyl-1,2,3,4-tetrahydroisoquinoline;

2-methyl-7-phenoxy-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

7-(4-methoxy)phenoxy-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

7-benzyloxy-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

7-hydroxy-2-methyl-4-(3-methyl)phenyl-1,2,3,4-tetrahydroisoquinoline;

4-(3-fluoro-4-methyl)phenyl-7-hydroxy-2-methyl-1,2,3,4-tetrahydroisoquinoline;

4-(4-fluoro-3-methyl)phenyl-7-hydroxy-2-methyl-1,2,3,4-tetrahydroisoquinoline;

4-(3,4-difluoro)phenyl-7-hydroxy-2-methyl-1,2,3,4-tetrahydroisoquinoline;

2,8-dimethyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

2,8-dimethyl-4-(4-fluoro)phenyl-1,2,3,4-tetrahydroisoquinoline;

4-(3,4-difluoro)phenyl-2,8-dimethyl-1,2,3,4-tetrahydroisoquinoline;

4-(3,5-difluoro)phenyl-2,8-dimethyl-1,2,3,4-tetrahydroisoquinoline;

2,8-dimethyl-4-(3-fluoro)phenyl-1,2,3,4-tetrahydroisoquinoline;

2,8-dimethyl-4-(4-fluoro-3-methyl)phenyl-1,2,3,4-tetrahydroisoquinoline;

4-(3-chloro-4-fluoro)phenyl-2,8-dimethyl-1,2,3,4-tetrahydroisoquinoline;

4-(3,4-dichloro)phenyl-2,8-dimethyl-1,2,3,4-tetrahydroisoquinoline;

4-(3-chloro)phenyl-2,8-dimethyl-1,2,3,4-tetrahydroisoquinoline;

4-(4-chloro)phenyl-2,8-dimethyl-1,2,3,4-tetrahydroisoquinoline;

4-(4-chloro-3-fluoro)phenyl-2,8-dimethyl-1,2,3,4-tetrahydroisoquinoline;

2,8-dimethyl-4-(4-methoxy)phenyl-1,2,3,4-tetrahydroisoquinoline;

4-(4-cyano)phenyl-2,8-dimethyl-1,2,3,4-tetrahydroisoquinoline;

2,8-dimethyl-4-(4-trifluoromethyl)phenyl-1,2,3,4-tetrahydroisoquinoline;

2,8-dimethyl-4-(4-methyl)phenyl-1,2,3,4-tetrahydroisoquinoline;

2-methyl-8-(N-methylamino)methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

8-(hydroxy)methyl-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

2-methyl-4-phenyl-8-sulfonamide-1,2,3,4-tetrahydroisoquinoline;

2-methyl-8-(N-methyl)sulfonamide-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

a4 8-methoxy-2-methyl-4-(4-methyl)phenyl-1,2,3,4-tetrahydroisoquinoline;

4-(3,5-difluoro)phenyl-8-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline;

4-(3-chloro)phenyl-8-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline;

4-(3,4-dichloro)phenyl-8-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline;

4-(4-chloro-3-fluoro)phenyl-8-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline;

4-(3-chloro-4-fluoro)phenyl-8-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline;

4-(3,5-difluoro)phenyl-2,7-dimethyl-1,2,3,4-tetrahydroisoquinoline;

4-(3-chloro-5-fluoro)phenyl-2,7-dimethyl-1,2,3,4-tetrahydroisoquinoline;

4-(3,5-difluorophenyl-1,2,7-trimethyl-1,2,3,4-tetrahydroisoquinoline;

(8-fluoro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-7-isoquinolinyl)-N-methylmethanamine;

2-methyl-4-phenyl-1,2,3,4-tetrahydro-7-isoquinolinyl)-N-methylmethanamine;

N-methyl(2-methyl-4-phenyl-1,2,3,4-tetrahydro-7-isoquinolinyl)-N-methylmethanamine;

8-hydroxy-2-methyl-4-phenyl-1,2,3,4-tetrahydro-7-isoquinolinecarbonitrile; and

(2-methyl-4-phenyl-1,2,3,4-tetrahydro-7-isoquinolinyl)methanol;

an oxide thereof, or a pharmaceutically acceptable salt thereof.

31. (Amended) A compound according to claim 1, selected from the group consisting of the following compounds:

	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
1.	Me	H	H	Me	H	H	H	H
2.	Me	H	H	Me	H	OMe	H	H
3.	Me	H	H	Me	H	F	H	H
4.	Me	H	H	Me	F	H	H	H
5.	Me	H	H	Me	F	F	H	H
6.	Me	H	H	Me	Me	F	H	H
7.	Me	H	H	Me	Cl	F	H	H
8.	Me	H	H	Me	Cl	H	H	H
9.	Me	H	H	Me	H	Me	H	H
10.	Me	H	H	Me	F	Me	H	H
11.	Me	H	H	Me	H	Cl	H	H
12.	Me	H	H	Me	F	Cl	H	H
13.	Me	H	H	Me	Cl	Cl	H	H
14.	Me	H	H	Et	H	H	H	H
15.	Me	H	H	Et	F	F	H	H
16.	Me	H	H	F	H	OMe	H	H
17.	Me	H	H	F	F	OMe	H	H

sub C1

	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
18.	Me	H	H	F	F	Me	H	H
19.	Me	H	H	F	F	Cl	H	H
20.	Me	H	H	F	F	F	H	H
21.	Me	H	H	F	Cl	H	H	H
22.	Me	H	H	CN	H	H	H	H
23.	Me	H	H	CF_3	H	H	H	H
24.	Me	Me	H	Me	H	H	H	H
25.	Me	H	Me	Me	H	H	H	H
26.	Me	H	F	Me	H	H	H	H
27.	Me	H	Me	F	H	H	H	H
28.	Me	H	OMe	Me	H	H	H	H
29.	Me	H	OH	Me	H	H	H	H
30.	Me	H	H	OCF_3	H	H	H	H
31.	Me	H	H	OMe	F	F	H	H
32.	Me	H	H	OMe	Me	F	H	H
33.	Me	H	H	OMe	F	Me	H	H
34.	Me	H	H	OMe	Me	H	H	H
35.	Me	H	H	O(Ph)	H	H	H	H
36.	Me	H	H	O(4-OmePh)	H	H	H	H
37.	Me	H	H	$O(CH_2Ph)$	H	H	H	H
38.	Me	H	H	OH	Me	H	H	H
39.	Me	H	H	OH	F	Me	H	H
40.	Me	H	H	OH	Me	F	H	H
41.	Me	H	H	OH	F	F	H	H
42.	Me	H	Me	H	H	H	H	H
43.	Me	H	Me	H	H	F	H	H
44.	Me	H	Me	H	F	F	H	H
45.	Me	H	Me	H	F	H	F	H
46.	Me	H	Me	H	F	H	H	H
47.	Me	H	Me	H	Me	F	H	H
48.	Me	H	Me	H	Cl	F	H	H
49.	Me	H	Me	H	Cl	Cl	H	H
50.	Me	H	Me	H	Cl	H	H	H
51.	Me	H	Me	H	H	Cl	H	H
52.	Me	H	Me	H	F	Cl	H	H
53.	Me	H	Me	H	H	OMe	H	H
54.	Me	H	Me	H	H	CN	H	H
55.	Me	H	Me	H	H	CF_3	H	H
56.	Me	H	Me	H	H	Me	H	H
57.	Me	H	CH_2NHMe	H	H	H	H	H
58.	Me	H	CH_2OH	H	H	H	H	H
59.	Me	H	SO_2NH_2	H	H	H	H	H
60.	Me	H	SO_2NHMe	H	H	H	H	H
61.	Me	H	OMe	H	H	Me	H	H
62.	Me	H	OMe	H	F	H	F	H
63.	Me	H	OMe	H	Cl	H	H	H
64.	Me	H	OMe	H	Cl	Cl	H	H

	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
65.	Me	H	OMe	H	F	Cl	H	H
66.	Me	H	OMe	H	Cl	F	H	H
67.	Me	H	H	Me	F	H	F	H
68.	Me	H	H	Me	F	H	Cl	H
69.	Me	Me	H	Me	F	H	F	H
70.	Me	H	H	Me	F	F	F	H
71.	Et	H	H	Me	H	F	H	H
72.	Me	H	F	CH_2Me	H	H	H	H
73.	Me	H	H	CH_2NH_2	H	H	H	H
74.	Me	H	H	CH_2NHMe	H	H	H	H
75.	Me	H	OH	CN	H	H	H	H
76.	Me	H	H	CH_2OH	H	H	H	H

32. (Amended) A compound according to claim 1, wherein the enantiomer is selected from the group consisting of the following compounds:

	R^1	R^2	R^3	R^4
1.	H	H	Me	F
2.	OMe	H	F	F
3.	Me	H	F	F
4.	H	H	Cl	F
5.	H	H	F	F
6.	Me	F	H	F
7.	Me	H	F	H
8.	Me	H	H	F